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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,436	12/22/2004	Hilde Azjin	TIP0015 US	7541

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PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,436	AZJIN ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 August 2007 has been entered.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

DETAILED ACTION

Claims 1, 3, 4 and 6-10 are cancelled. Claims 2 and 5 are pending and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 2 and 5 under 35 U.S.C. §112, second paragraph, as being indefinite is **maintained**. The claims do not particularly point out the following:

(1) what is the wild type residue that is mutated to glycine at position 194?

(2) which strain of HIV is position 194 in reference to?

Due to the error-prone replication of HIV, there are many quasi species with different nucleotide and amino acid sequences. Especially when insertion or deletion mutations occur during viral replication, the sequences of the quasi species differ substantially from one another that a skilled artisan would not know whether one position number in one strain is referring to the same position in another strain. Therefore, position numbers in the absence of a reference strain number is vague and

indefinite. Furthermore, simply referring to a mutation at a position without a reference sequence is vague and indefinite. One skilled in the art would not know what is the wild type amino acid residue at each position because of the existence of so many HIV-1 subtypes and strains. Claims 2 and 5 lack the recitation of the wild type residues, which is confusing because one would not know how to discern a mutant amino acid from a wild type at each position when the comparison of the amino acids is not based on a parental isolate sequence.

Furthermore, the method steps are arranged in a non-operative order, *i.e.* one skilled in the art cannot perform (iii), correlating a mutation to a change in an HIV drug susceptibility, before carrying out the steps (iv) and (v).

The rejection of claims 2 and 5 under 35 U.S.C. §112, first paragraph, as containing new matter is **withdrawn** in response to the amendment.

The rejection of claims 2 and 5 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **maintained** for reasons of record. Applicants did not address this rejection in the response filed on 17 August 2007.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 2 and 5 under 35 U.S.C. §103(a) as being obvious over Stein *et al.* (1994) in view of Servais *et al.* (February, 2001) is **maintained**. Applicant's arguments have been fully considered but are not persuasive.

The instant claims are directed to a method for evaluating the effectiveness of an HIV reverse transcriptase inhibitor as an anti-HIV therapy for a patient infected with at least one mutant HIV strain comprising:

(i) collecting a sample from an HIV-infected patient;

(ii) determining whether the sample comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation at the position 194, wherein the wild type amino acid is mutated to glycine;

(iii) correlating the presence of said at least one mutation of step (ii) to a change in effectiveness of said HIV reverse transcriptase inhibitor;

(iv) determining the effectiveness of said HIV reverse transcriptase inhibitor; and

(v) comparing the effectiveness of said inhibitor in samples containing said reverse transcriptase mutation with samples no containing said mutation.

Stein *et al.* disclose sequence analysis of HIV RT from HIV patients comprising collecting a sample from an HIV-infected patient; determining whether the sample

comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation at position 194; and correlating the presence of the mutations to a change in effectiveness or susceptibility of AZT, a reverse transcriptase inhibitor (page 117, Table II).

Stein *et al.* do not disclose the specific amino acid change to glycine (G) at position 194. However, Servais *et al.* disclose that the 194G mutation is found in the patient isolates in an assay for HIV-1 drug resistance mutations.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the drug-resistance mutation profiles taught by Stein *et al.* and Servais *et al.* such that the modified method has a more comprehensive mutation profile. One having ordinary skill in the art would have been motivated to do this so that the new mutation profile contributes to a more complete and accurate drug evaluation. Thus, claims 2 and 5 are obvious over Stein *et al.* in view of Servais *et al.*

Applicants argue that Stein *et al.* do not teach the HIV reverse transcriptase mutant containing a mutation 194G and that Servais *et al.* merely identifies a drug resistant mutation 194G, which does not give rise to an analysis that looks for such a mutation in a sample as the basis for a drug therapy and does not suggest a comparison with a sample that does not contain such mutation. However, this argument mischaracterizes the rejection because Stein *et al.* was offered for teaching the claimed correlation of the effectiveness of a HIV reverse transcriptase inhibitor to a mutation at position 194. Servais *et al.* further disclose the mutation to glycine at

position 194. Thus, the obviousness of the combination does not hinge on whether Servais *et al.* suggest an analysis that looks for such a mutation in a sample and a comparison with a sample that does not contain such mutation. Rather, the motivation to combine the references was to use the Servais reference's glycine residue as the clue for mutation in an assay to associate the mutation detected in patient HIV proviral DNA with the effectiveness the reverse transcriptase inhibitor, as taught by Stein *et al.* Therefore, a *prima facie* case of obviousness is properly established.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
10 October 2007

Louise Humphrey, Ph.D.
Assistant Examiner